REMARKS / ARGUMENTS

Claims 1-44 remain in this application. All claims stand rejected. Claims 1, 22 and 42 have been amended herein.

1. AMENDED CLAIM 1 IS NOVEL OVER US 5,322,057 TO RAABE

Anticipation requires complete identity between the prior art reference and the claimed subject matter.

Amended claim 1 is not anticipated by US 5,322,057 to Raabe as Raabe does not disclose:

> ***(a) a housing adapted to be carried by a patient breathing without the assistance of a respirator and sized to fit within the patient's hand while said device is in use by the patient;***

Raabe discloses an ultrasonic nebulizer for use with a respirator which mechanically breaths for individuals unable to breath unassisted. This nebulizer unit is not a housing adapted to be carried by a patient breathing without a respirator. Moreover, the Raabe nebulizer is not sized to fit within the patient's hand while the device in use by the patient. These limitations have been placed in the body of the claim, reflecting the examiner's comments on Page 18 of the Office Action.

Furthermore, and significantly, Raabe does not disclose a monitor whose operation is

> *characterized in that the monitor provides said signal at a trigger point which is correlated to the end of the exhalation part of the breath cycle.* (Emphasis added).

As stated in Raabe:

> *The present invention is based upon the nebulization of medicine **during and synchronized with the exhalation portion of each breath of the breathing cycle** to fill the airline leading from the nebulizer to the patient with a standardized dose of medicinal aerosols that are delivered to the lung by the force of the flow of breathing gas (oxygen enriched air) delivered by the respirator during the inhalation portion of the breathing cycle. (Col. 2, line 25-33)(emphasis added).*

The specification reiterates that the operation of the nebulizer is "during the **exhalation phase** of the respirator" is pointed out at Col. 4, lines 2-10.

The examiner interprets col. 2, line 67- col. 3, line 2 as providing the claim limitation of claim 1 that "*said signal at a trigger point which is correlated **to the end of the exhalation part of the breath cycle.***" However, that passage again repeats that triggering and nebulization occurs ***during*** exhalation:

> The nebulizer has a reservoir of capacity sufficient to enable several hours of continuous treatment and with provision to prevent the settling of suspensions or mixtures without creating nebulization-destroying turbulence, and provides a precisely measured **volume of medicinal aerosol generated during patient exhalation** in a manner to reach the patient at the precise moment when inhalation begins.

Thus, Raabe discloses generation of an aerosolized dose of medicament at the commencement of the exhalation cycle, whereas the instant invention generates and releases the dose this ***at the end of the exhalation part of the breath cycle***. Thus the instant invention functions in a different fashion than the prior art.

This timing distinction is not trivial. By generating the aerosolized dose when it does, the instant invention overcomes problems associated with user error, which is not a problem when a patient who is unable to breath unassisted is relying on a machine to artificially regulate their breathing, as in Raabe. Particularly, in the present invention, the patient is unable to exhale into the device and negatively impact the aerosolized dose prior to administration of the dose to the patient because the dose is not generated until after the exhalation phase ends. In a patient used device, the mouthpiece may be blown into if used improperly. In Raabe, such a problem doesn't exist because the exhaled air is drawn through a separate tube 73.

Moreover, if aerosolization commenced later in Raabe, i.e., at the end of the exhalation cycle, it could interfere with the functioning of the mechanical respirator by increasing the tidal flow of gas into a patient's lungs, As note in the discussion of the prior art in column 2, lines 12-24, this was one of the very problems Raabe was attempting overcame by correlating nebulization with the beginning of the exhalation phase.

Due to the differences in these aspects, Raabe and claim 1 do not possess the identity of features required to establish a case of anticipation under 35 USC 102. Claims 1-3, 7-8, 15-18, 20-22, 28-30, 32, 36-37 and 41 each depend on claim 1, and are not anticipated for the same reasons.

With regard to claim 7, Raabe discloses that the solenoids 7/6 are triggered at the beginning of the exhalation phase. At this point in the breathing cycle, the lungs are full with air. Claim 7 is not identical to the device disclosed in Raabe, and is not anticipated by Raabe for this additional reason.

Claims 15 and 16 both depend from claim 12, which in turn depends on claim 9, which in turn depends from claim 8. At page 11 of the 4/6/04 Office Action, the examiner found that Raabe failed to disclose an active memory store as in claim 9. Therefore, as a matter of law, claims 9, 12, 15 and 16 cannot be anticipated by Raabe.

Claims 17-21 depend from claim 16. These claims are, as a matter of law, novel for the same reasons indicated why claim 16 is novel.

Further claim 21, requires that

> *a selector comprising a multiple fire mechanism for* ***multiple actuation of the actuator****, wherein each actuation releases a portion of the optimum amount of medicament.*

The Raabe reference discloses a control unit 80, connected to a microprocessor 9, which controls the functioning the nebulizer 10. The nebulizer valves 6/7 are controlled by the microprocessor 9. Raabe states that the valves 6 and 7 can be moved between an open position, wherein nebulizing nozzles 22 aerosolize the medicament fed from reservoir 26 through liquid feed tubes 24, and a closed position where they are not. (Col. 4, lines 2-13; lines 23-29.) The microprocessor calculates the amount of time which the solenoids 6 would have to be activated in order to introduce the desired amount of aerosol into the inhalation tube 71 (col. 5, line 20-23) once triggered at the beginning of the exhalation phase. Nebulization continues from the three nozzles until a standardized dose has been produced. (col. 5, lines 39-61.) Raabe states that the nozzles can be turned on simultaneously, or one at a time to produce the desired charging flow volume during a portion of the exhalation period. (Col 6, lines 28-34).

In either case, the aerosolized dose in Raabe is formed from **multiple solenoids/nozzles generating a single dose**, rather than the actuation of a given actuator **multiple times**, as called for in claim 21. The advantage of this is that the claimed multiple actuation mechanism can use a single sized metering chamber in a single valve and still have the ability to increase or decrease the delivered dosage, offering cost savings advantages in manufacturing. For this additional reason, claim 21 is not anticipated.

Claim 22 has been amended to recite a pressurized liquid propellant. The amendment is not made to distinguish Raabe but to better define the invention of claim 22. However, Raabe does not describe the additional features of claim 22. For this additional reason, the claim is not anticipated by Raabe.

Regarding claim 29, the claim recites an energy store for storing energy which energy is releasable to activate the release mechanism of the medicament container. The examiner refers to the compressed air inlet 2 and the compressed gas conduit 4, and the fixed volume chamber 82. The air inlet attaching to conduit 2 provided the nebulizing gas flow for the nebulizing nozzles 22, whereas the fixed volume chamber provides decay gas

flow. None of these components constitute *an energy store for storing energy which energy is releasable to activate the release mechanism of the medicament container.* In short the gas present in these lines 2/4 or chamber 82, do not operate the solenoids 6/7. The control mechanism for 6/7 has no energy store as part of the actuator, instead being operated through an external power supply (note the non-referenced power cord in Figure 1). The Raabe device lacks the requisite energy store and for this additional reason lacks identity with claim 29.

Claims 30 and 32 are dependent on claim 29 and are novel for the same reasons as claims 29 mentioned above.

Regarding claim 36, the examiner states that Raabe has a safety mechanism to prevent unintended multiple firing of the actuator, citing col. 5, lines 62-68). The safety mechanism described, pressure sensor 15, does not prevent multiple firing, but rather shuts off the nebulizer *in the event that pressure within the inhalation tube 71 builds to an excessive level or if inhalation begins*. The pressure sensor 15 could not prevent multiple firings unless one of these events occurred, and therefore does not meet the limitations of claim 36. Claim 36 is novel for this additional reason.

Regarding claim 37, it is novel for the same reasons as claim presented above for claim 36. Additionally though, contrary to the statement of the examiner, there is no time delay in "pressure sensor" 15, the safety mechanism in Raabe pointed to by the examiner. The pressure sensor would not act to preclude action of the device unless (i) *pressure within the inhalation tube 71 builds to an excessive level or* (ii) *inhalation begins*. Raabe does not describe a safety mechanism that "*imposes a time delay between successive actuations of the actuator*" and therefore there is no identity between the claim and the reference for this additional reason.

Concerning Claims 42-44, the method disclosed in claims 42-44 is not anticipated through inherent functioning of Raabe, as these claims require that the monitor generate a signal at a trigger point, *characterized in that said trigger point is correlated to the end*

of the exhalation part of the breath cycle. As explained previously, this distinction leads to the conclusion that the claimed subject matter is not identical to the method inherently carried out by the Raabe device, and therefore, the claim and those claims dependent thereon are not anticipated by Raabe.

2. THE CLAIMED INVENTION IS NON-OBVIOUS OVER RAABE

As stated above, the Raabe reference does not disclose

> *(b) a monitor for monitoring the breath cycle of a patient positioned within said housing;...*

characterized in that the monitor provides said signal at a trigger point which is ***correlated to the end of the exhalation part of the breath cycle.*** (emphasis added).

The standing rejections of the claims as being obvious over the Raabe reference alone are traversed for the same reasons mentioned above for the claims being novel over Raabe. Raabe initiates medicament generation at the **beginning of the exhalation phase** so as to fill the inhalation line with aerosolized medicament without impacting the operation of a respirator by exerting excess pressure into the inhalation lines. There is nothing in Raabe to teach or suggest modifying the timing of aerosolization repeatedly raised in the reference to that suggested by the applicants.

Moreover, the applicant's use of this approach of timing aerosolization to the end of the exhalation phase affords various significant advantages in a hand held patient operated device. For example, breath operated inhalers operating on reaching a threshold pressure to trigger to actuate release of medicament, will often rely on a sensor for measuring pressure drop. Pressure sensors set are desirably mass produced and in mass production, the tolerances that the sensors must meet are often difficult to set in a uniform fashion. The sensitivity of individual pressure sensors may fluctuate widely over the course of a manufacturing run, due to slight variations of materials, etc. These tolerances would lead to a wide variation in measuring a particular positive or negative airflow value, and

therefore, must be calibrated to be made uniform by after-manufacturing modification. Calibrating each sensor independently undesirably adds to the cost of the device.

The present invention overcomes the need to undergo this post-manufacturing calibration. A particular pressure threshold measurement is not needed when measuring the end of the exhalation phase. All that is being determined is that the phase has ended, and as such, all sensors will work equally as well to measure this phenomenon, regardless if they would measure actual pressure values differently. As such, the minor physical differences in the sensors approach are irrelevant. Thus, triggering actuation at the claimed time permits the use of less expensive mass produced sensors without having to individually calibrate each sensor.

Moreover, pressure drop sensors within an inhaler are subject to clogging by the medicament after repeated use of the device. This phenomenon was described in Raabe (col. 7, 25-45). Clogging in the pressure drop sensor leads to variations in measurements of pressure passing through the pressure drop, for example as an orifice becomes more restricted due to material deposition. This clogging ultimately effects the operation of the breath sensor on the device as the measuring sensitivity deviates from its original state.

While this constriction due to clogging may adversely affect a system dependent upon measuring the actual pressure value, it does not affect a device where measuring a threshold pressure value is not required, such as the instant device. Using an end-of-exhalation approach, as in the claimed invention, allows the actuator to be fired at a point where the pressure is no longer measured. All the sensor needs to indicate is the "turning point" at the end of exhalation. The measurement of a particular value or positive of negative inspiratory threshold is no longer critical to operating the device. In the case of a portable, user operated device, this change in approach allows an end of use device to be functional for its entire life without experiencing a decline in function of its breath operated feature due to clogging.

A further advantage of the present invention over that described in Raabe is that the potential for patient error is eliminated. It can be appreciated that in a breath operated inhalation device, the patient exhaling through the device after the device has released the medicament plume will cause the aerosolized dose to either be blown out of the device (rather than being inhaled) or negatively impacted in terms of its fine particle fraction by the humidity of the exhaled breath. This problem is eliminated in the instant invention by correlating the timing of the generation and release of the medicament plume to the end of the exhalation phase of the breathing cycle. At this point the lungs are empty and exhalation through the device is not possible.

Note Raabe avoids this issue, as the resuscitator is breathing for the patient and mechanically controls the tidal flow of breathing gas. Further, Raabe states that the inhalation port 76 is closed beginning at exhalation phase, and is only opened upon the start of the inhalation phase.

Because Raabe does not disclose or suggest the claimed invention, and in light of the significant advantages afforded by the instant invention, it is respectfully asserted that Claims 1-44 are non-obvious over Raabe.

3. THE CLAIMED INVENTION IS NON-OBVIOUS OVER RAABE IN LIGHT OF GOODMAN

Goodman describes mechanisms for improving aerosol delivery but does not describe or suggest correlating the generation of such particles to the end of the exhalation part of the breath cycle as claimed in the instant claims. As neither Goodman nor Raabe disclose those elements lacking in Raabe, a prima facie case of obviousness cannot be established. The applicant respectfully requests that the rejection of claims 9-14, 38 and 39 be withdrawn.

4. THE CLAIMED INVENTION IS NON-OBVIOUS OVER RAABE IN LIGHT OF LANDIS

Landis describes a breath operated inhaled triggered by inhalation reaching a given threshold, and also a manual override in case the device fails to operate as designed. It does not describe or suggest a using a monitor for generating a signal to a release mechanism correlated to the end of the exhalation part of the breath cycle as claimed in the instant claims. As neither Landis nor Raabe disclose those elements present in the claimed invention, a prima facie case of obviousness cannot be established. Further, applicants disagree with the examiner's finding that it would be obvious to select from the prior art a metered dose inhaler manual override that allows a patient operating a metered dose inhaler to self-actuate their inhaler in case the breath operated function fails, and incorporate this into an attachment on a respirator which is breathing for a patient unable to breath unaided, as in Raabe. We respectfully suggests that the patient would likely incapable of using the override in their particular state, which one would assume to be unconsciousness or paralysis. The use of the override would then pass to the attendant, who would be required to manipulate this override repeatedly over hours of therapy, which would be a highly unlikely proposition. In addition, as mentioned in detail above, the non-obviousness of these claims is further bolstered due to advantages in the device in terms of manufacture and function provided by the claimed elements. The applicant respectfully requests that the rejection of claim 40 be withdrawn.

4. THE CLAIMED INVENTION IS NON-OBVIOUS OVER RAABE IN LIGHT OF TARGELL

Applicant disagrees with the finding that the invention as described in Claims 25-27 is obvious over Raabe in view of Targell. Neither Raabe not Targell disclose

> *(b) a monitor for monitoring the breath cycle of a patient positioned within said housing;...*

characterized in that the monitor provides said signal at a trigger point which is ***correlated to the end of the exhalation part of the breath*** *cycle.* (emphasis added).

Therefore, a prima facie case of obviousness can not be established.

Further, Targell describes a pump with a fixed metering volume. . It is not a metering chamber for metering the release of medicament having a *variable metering volume.* The volume metered per stroke is established in the factory when element 30 is created. The advantage of the variable metering volume approaches claimed in claims 25-27 is the ability to easily adjust the metered volume of medicament in the device to provide a greater flexibility in dosating a medicament without having to have separate sizes of components having fixed metering volumes.. This "once size fits all" advantage is incapable of being achieved in the same way with Targell.

For these reasons, withdrawal of the rejection of claims 25, 26 and 27 is respectfully requested.

CONCLUSION

For the reasons provided above Raabe does not anticipate the claimed presented herin. Further, Raabe does not render the claims obvious, even when considered in light of the knowledge of one of ordinary skill, or in light of the Goodman, Landis or Targell references.

In light of these amendments, all issued raised by the examiner to date have been addressed. As such, the claims are asserted to be in a condition for allowance. Applicant requests that a timely Notice of Allowance be issued in this case. If any matters exist that preclude issuance of a Notice of Allowance, the examiner is requested to contact the applicant's representative at the number indicated below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge any fees or credit any overpayment, particularly including any fees required under 37 CFR Sections 1.16 and/or 1.17, and any necessary extension of time fees, to deposit Account No. 07-1392.

Respectfully submitted,

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